Remarks

Claims 1-24 were previously pending in the subject application. By this amendment, the applicants have amended the specification to include materials disclosed in co-pending U.S. Application Serial No. 10/274,829 (Application Publication No. 20040076681) which was incorporated by reference in its entirety. The applicants have also amended claims 1 and 2 and canceled claims 12-24. No new subject matter has been added by this amendment. Claims 1 and 2 have been amended to clarify the claimed subject matter. Claims 12-24 have been canceled as being drawn to non-elected subject matter. Support for the amendment to specification and claims 1 and 2 can be found throughout the specification including, for example, at page 30. Accordingly, claims 1-11 are now before the Examiner for consideration.

The amendments set forth herein should not be interpreted to indicate that the applicants have agreed with, or acquiesced to, the rejections set forth in the outstanding Office Action. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 2-4 have been rejected under 35 U.S.C. §112, first paragraph. The applicants respectfully submit that these claims are fully enabled by the subject specification. However, as noted above, the applicants have amended the subject specification to incorporate disclosure of a copending U.S. Application Serial No. 10/274,829 (hereinafter the '829 application), which contains information regarding the mechanism for release of an entrapped surrogate marker from a nanoparticle. It is a basic premise of patent law that the claims must be supported by and interpreted in accordance with the disclosure of the invention in the application. See *Allen Archery Inc. v. Browning Mfg. Co.*, 819 F.2d 1087 (Fed. Cir. 1987). The Federal Circuit has recognized that "a patent applicant may complete his disclosure, and hence satisfy 35 U.S.C. §112, by reference to an earlier or concurrently filed U.S. application." See *In re Fouche*, 439 F.2d 1237, 1238 (CCPA 1971). To this end, the applicants respectfully submit that the '829 application provides specific teachings regarding the uncapping of an end-cap from a nanoparticle through an interaction between the detecting means attached to the end-cap and the target analyte/biomarker (see paragraphs 45-48 of the '829 application), which were incorporated by reference in the subject application. Accordingly, the currently amended specification

contains sufficient information to support claim 2. Thus, the applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1, 2, and 5-11 have been rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps. The applicants respectfully submit that claim 1 is not indefinite because claim 1 does disclose the release of a surrogate marker upon detection of a target analyte/biomarker. In order to expedite prosecution, claim 1 has been amended herein to clarify that the sensor technology can detect a surrogate marker released from the nanostructure-based assembly in the container and that detection of the surrogate marker by the sensor technology indicates the presence of the target analyte/biomarker in the bodily fluid sample.

Claims 1-11 have been rejected under 35 U.S.C. §112, second paragraph as indefinite because the intended sensor technology is unclear. The applicants submit that, given the teachings at pages 25-29 under the heading of "Sensor Technology" in the subject specification, one of ordinary skill in the art would understand that the sensor technology may be a SAW sensor, BAW sensor, plate acoustic wave device, electrochemical sensor, artificial nose or tongue, semiconductive gas sensor, *etc.*, so long as it can detect the presence of a surrogate marker released from a nanostructure-based assembly of the invention.

Claim 2 has been rejected under 35 U.S.C. §112, second paragraph as indefinite. The applicants respectfully submit that the use of the phrase "wherein when the means for detecting the target analyte/biomarker is in the presence of the target analyte/biomarker, the end-cap is displaced from the first end to release the surrogate marker" does not render claim 2 indefinite. However, as noted above, in order to expedite prosecution, claim 2 has been amended to clarify that binding of "the means for detecting the target analyte/biomarker" to the target analyte/biomarker causes displacement of the end-cap.

The Office Action also indicates that claim 10 lacks antecedent basis. The applicants submit that there is sufficient antecedent basis for "the surrogate marker," which is introduced in section (b) of claim 1.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

Claims 1, 5, 8, and 9 have been rejected under 35 U.S.C. §102(b) as anticipated by Fu (U.S. Patent No. 6,598,459). The applicants note that the Fu reference issued within one year of the filing of the subject application and, thus, is not available as prior art under 35 U.S.C. §102(b). Nevertheless, to the extent that Fu is available at all as a prior art reference, the applicants respectfully submit that the claimed invention is neither anticipated by, nor rendered obvious in view of, Fu.

The subject application teaches a unique method for detecting *ex vivo* the presence of a target analyte/biomarker in a sample of bodily fluid. Specifically, to detect a target analyte/biomarker *ex vivo*, stand-alone nanostructure-based assemblies are first mixed with a sample of bodily fluid. The nanostructure-based assembly, which is wholly independent from the sensor technology, comprises a surrogate marker that is released upon detection of a target analyte/biomarker in the sample of bodily fluid. Thus, the nanostructure-based assembly is a carrier for the surrogate marker. Only after mixing the nanostructure-based assembly with the bodily fluid is the sensor technology then applied to the mixture to detect, if present, the surrogate marker.

In contrast, Fu only teaches the use of a sensor to detect odorant molecules in air. Fu neither discloses nor suggests the use of stand-alone nanostructure-based assemblies as carriers for surrogate markers, let alone mixing such nanostructure-based assemblies with a bodily fluid sample. Rather, as indicated in the Office Action, Fu teaches incorporating nanotubes in a sensor (see col. 2, lines 38-44), where the nanotubes increase sensor surface area for detecting an odorant molecule. Fu fails to disclose using nanostructure-based assemblies that are independent from sensor technology.

Further, as noted in the Office Action, a reactive material, such as a protein (see col. 3, lines 47-51), can be provided in the aerogel/polymer layer of the Fu sensor (see col. 6, lines 59-65) to react with a biological agent to chemically generate an odorant molecule. In contrast, the surrogate markers of the invention, which are released from nanostructure-based assemblies that independent from sensor technology, do not need to react with the target analyte/biomarker to enable detection via sensor technology. Accordingly, the applicants respectfully submit that the Fu reference does not teach or even suggest their claimed methods.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

In *Dewey & Almy Chem. Co. v. Mimex Co.*, Judge Learned Hand wrote:

> No doctrine of the patent law is better established than that a prior patent . . . to be an anticipation must bear within its four corners adequate directions for the practice [of the subsequent invention] . . . if the earlier disclosure offers no more than a starting point . . . if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation. 124 F.2d 986, 990; 52 USPQ 138 (2nd Cir. 1942).

The applicants respectfully submit that Fu reference does not disclose or suggest each and every element of the claimed invention. For example, Fu fails to disclose or suggest mixing nanostructure-based assemblies with a bodily fluid sample, wherein the assemblies are carriers for surrogate markers that are released upon detection of a target analyte/biomarker. Therefore, reconsideration and withdrawal of the rejection under §102 is respectfully requested.

Claim 10 has been rejected under 35 U.S.C. §103(a) as obvious over Fu in view of Lewis *et al.* #1 (U.S. Patent no. 5,571,401). The applicants respectfully traverse this rejection because neither reference teaches or suggests the claimed methods.

The shortcomings of the Fu reference have been discussed above in detail. The Lewis *et al.* #1 reference merely discloses the use of chemiresistor sensors for detecting an analyte in a fluid sample. The Lewis *et al.* #1 reference does not describe or even suggest the use of nanostructure-based assemblies as carriers for detectable surrogate markers that indirectly signal

the presence of target analytes/biomarkers. Further, there is no description by Lewis *et al.* #1 that such nanostructure-based assemblies are independent from sensor technology used to detect the surrogate markers. The skilled artisan would have had no reason to look to the Lewis *et al.* #1 reference for guidance in developing the claimed methods for detecting target analytes/biomarkers *ex vivo*. Under these circumstances, the subject invention cannot reasonably be said to be obvious.

As a matter of law, a finding of obviousness is proper only when the prior art contains a suggestion or teaching of the claimed invention. Here, it is only the applicants' disclosure that provides such a teaching, and the applicants' disclosure cannot be used to reconstruct the prior art for a rejection under §103. This was specifically recognized by the CCPA in *In re Sponnoble*, 56 CCPA 823, 160 USPQ 237, 243 (1969):

> The Court must be ever alert not to read obviousness into an invention on the basis of the applicant's own statements; that is we must review the prior art without reading into that art appellant's teachings. *In re Murray*, 46 CCPA 905, 268 F.2d 226, 112 USPQ 364 (1959); *In re Sprock*, 49 CCPA 1039, 301 F.2d 686, 133 USPQ 360 (1962). The issue, then, is whether the teachings of the prior art would, in and of themselves and without the benefits of appellant's disclosure, make the invention as a whole, obvious. *In re Leonor*, 55 CCPA 1198, 395 F.2d 801, 158 USPQ 20 (1968). (Emphasis in original)

Combining prior art references without evidence of a suggestion, teaching, or motivation simply takes the inventors' disclosure as a blueprint for piecing together the prior art to defeat patentability--the essence of hindsight. *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985). Additionally, the Court of Customs and Patent Appeals has stated, "[i]n determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 458 F.2d 1013, 1016 (CCPA 1972).

The current invention provides novel methods for the *ex vivo* detection of target analytes/biomarkers in a bodily fluid sample using nanostructure-based assemblies as carriers for

surrogate markers, where the surrogate markers are detected using sensor technology that is independent of the assemblies. The cited art neither discloses nor suggests the use of such nanostructure-based assemblies. One of ordinary skill in the art would have had no motivation to modify the cited teachings without the guidance of the applicants' disclosure. Without such a motivation, no *prima facie* case of obviousness has been made. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection set forth under 35 U.S.C. §103.

Claims 6 and 7 have been rejected under 35 U.S.C. §103(a) as obvious over Fu in view of Lewis *et al.* #2 (U.S. Patent No. 6,467,333). The applicants again respectfully traverse this ground for rejection because the cited references, alone or in combination, do not disclose or suggest the advantageous methods for the *ex vivo* detection of target analytes/biomarkers in a bodily fluid sample.

The shortcomings of the Fu reference have been discussed above in detail. The Lewis *et al.* #2 reference merely describes certain endogenous analytes (such as volatile sulfur compounds, see col. 8, lines 40-65) detectable in exhaled breath that are indicative of certain clinical conditions (such as halitosis). This has no relevance to the methods of the subject invention, which claims nanostructure-based assemblies for mixture with a bodily fluid sample *ex vivo*, where detection of a target analyte/biomarker causes the release of a detectable surrogate marker from an assembly that is not endogenously produced by the patient. There is no reason to think that one skilled in the art would be motivated to look to either the Lewis *et al.* #2 or the Fu references for guidance in developing methods for detecting target analytes/biomarkers *ex vivo* using the currently nanostructure-based assemblies.

As noted above, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation to combine the teachings of the cited references to arrive at the claimed invention. *Ex parte Clapp*, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985). The current invention utilizes nanostructure-based assemblies and surrogate markers that are not disclosed in either of the cited references. Thus, one of ordinary skill in the art would have had no motivation to modify the cited teachings without the guidance of the applicants' disclosure. Without such a motivation, no *prima facie* case of obviousness has been made. Accordingly, the applicants

respectfully request reconsideration and withdrawal of the rejection set forth under 35 U.S.C. §103.

Claim 11 has been rejected under 35 U.S.C. §103(a) as obvious over Fu in view of Massey *et al.* (U.S. Patent No. 6,598,459). The applicants respectfully traverse this rejection because the cited references neither disclosure nor suggest the advantageous methods for detecting target analytes/biomarkers *ex vivo*.

The shortcomings of the Fu reference have been discussed above in detail. The Massey *et al.* reference merely discloses the use of graphite-based nanotubes in an assay device. The Massey *et al.* reference fails to describe, let alone suggest, nanostructure-based assemblies as carriers for surrogate markers, where the markers are released from the nanostructure-based assembly upon detection of a target analyte/biomarker. Further, the Massey *et al.* reference fails to disclose mixing such nanostructure-based assemblies with a bodily fluid sample and applying sensor technology to the mixture to detect any surrogate markers, where the surrogate markers indirectly indicate target analyte/marker presence in the sample. Thus, the Massey *et al.* reference fails to remedy, or even address, the defects previously noted in the Fu reference. Since there is no suggestion or motivation in either reference that would lead a person skilled in the art to arrive at the currently claimed methods, the subject invention cannot reasonably be said to be obvious. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103 based on the Fu and Massey *et al.* references.

In view of the foregoing remarks and amendment, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

Margaret H. Efron
Patent Attorney
Registration No. 47,545
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: Saliwanchik, Lloyd & Saliwanchik
P.O. Box 142950
Gainesville, FL 32614-2950

MHE/la

J:\uf\378c1\pto\UF-378C1.amend doc/DNB/la